Incidence Trends in the Anatomic Location of Primary Malignant Brain Tumors in the United States: 1992–2006

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Key words

- Astrocytoma
- Brain neoplasm
- Epidemiology
- Glioma
- Glioblastoma multiforme
- Incidence
- Location

Abbreviations and Acronyms

AA: Anaplastic astrocytoma

AAIR: Age-adjusted incidence rates

APC: Annual percent changes

CCR: California Cancer Registry

CNS: Central nervous system

GBM: Glioblastoma multiforme

ICDO-3: International Classification of Disease for

Oncology, Third Edition

LAC: Los Angeles County Cancer Surveillance Program

SEER: National Cancer Institute's Surveillance, Epidemiology, and End Results WHO: World Health Organization

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INTRODUCTION

Over the last 3 decades, several population-based studies have reported an overall increase in the incidence of malignant primary brain tumors (I, 4, 6-9, II, I4). Although it has been generally accepted that this phenomenon is at least in part accounted for by higher detection rates associated with the increasing frequency and sensitivity of diagnostic imaging, it remains to be determined whether the true incidence of primary central nervous system (CNS) tumors is independently increasing as a result of environmental factors (I, II, I8).

- BACKGROUND: This study sought to determine incidence trends of the anatomical origin of primary malignant brain tumors.
- METHODS: Incidence data for histologically confirmed brain tumors were obtained from the Los Angeles County Cancer Surveillance Program (LAC), the California Cancer Registry (CCR), and the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program for 1992 to 2006. Ageadjusted incidence rates (AAIR) and annual percent changes (APC) were calculated by histologic subtypes and anatomic subsites. Statistical analyses were performed using the SEER*Stat analytic software and SAS statistical software.
- RESULTS: Increased AAIRs of frontal (APC +2.4% to +3.0%, $P \le 0.001$) and temporal (APC +1.3% to +2.3%, $P \le 0.027$) lobe glioblastoma multiforme (GBM) tumors were observed across all registries, accompanied by decreased AAIRs in overlapping region GBMs (-2.0% to -2.8% APC, $P \le 0.015$). The AAIRs of GBMs in the parietal and occipital lobes remained stable. The AAIR of cerebellar GBMs increased according to CCR (APC +11.9%, P < 0.001). The AAIR of all gliomas, which includes all anatomical subsites, decreased (-0.5% to -0.8% APC, $P \le 0.034$). Low-grade and anaplastic astrocytomas demonstrated decreased AAIRs in the majority of brain regions.
- CONCLUSIONS: Data from 3 major cancer registries demonstrate increased incidences of GBMs in the frontal lobe, temporal lobe, and cerebellum, despite decreased incidences in other brain regions. Although this may represent an effect of diagnostic bias, the incidence of both large and small tumors increased in these regions. The cause of these observed trends is unknown.

Although many previous reports have analyzed trends in the overall incidence of gliomas and various glioma subtypes, few recent studies have examined these trends according to the anatomical subsites of primary malignant brain tumors over the last several decades (2, 10). Furthermore, no recent studies have analyzed populationbased incidence trends by both tumor grade subtype and anatomic location. Given the increasing trends of primary malignant brain tumors, we sought to determine whether any notable trends in the anatomical topography of primary CNS tumors have occurred. Data from 3 major populationbased cancer registries were reviewed to identify any trends in the incidence of primary malignant brain tumors, their location of origin, and various demographic risk factors. The current study is the first to analyze population-based incidence trends of malignant brain tumors according to anatomical parameters.

CLINICAL MATERIALS AND METHODS

Data used in our analysis were obtained from 3 sources, the largest of which is the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program (16). A signed limited-use data agreement was obtained to access these data. This program includes incidence and population data associated by age, gender, race/ethnicity, and year of diagnosis. Thirteen

Table 1. Demographic Characteris	tics of Patients Hai	rboring Gliomas	in 3 Major Tumo	or Registries, 199	2 to 2006		
	LA Cou	LA County		CCR		SEER 12 Registries	
	Number	%	Number	%	Number	%	
Total number	5736	100.0	10,412	100.0	22,419	100.0	
Sex							
Male	3154	55.0	5864	56.3	12,651	56.4	
Female	2582	45.0	4548	43.7	9768	43.6	
Age							
0–19	476	8.3	711	6.8	1477	6.6	
20–64	3141	54.8	5880	56.5	12,386	55.2	
65+	2119	36.9	3821	36.7	8556	38.2	
Ethnicity							
Non-Hispanic white	3410	59.4	6776	65.1	18,658	83.2	
Hispanic white	1514	26.4	2057	19.8	1288	5.7	
Black	402	7.0	603	5.8	1161	5.2	
Asian/other	410	7.1	976	9.4	1312	5.9	
Location							
Frontal lobe	1434	25.0	2653	25.5	5781	25.8	
Temporal lobe	1045	18.2	1938	18.6	4548	20.3	
Parietal lobe	766	13.4	1449	13.9	3125	13.9	
Occipital lobe	147	2.6	291	2.8	762	3.4	
Overlapping	1238	21.6	2238	21.5	3897	17.4	
Cerebellum	124	2.2	203	1.9	344	1.5	
Brainstem	249	4.3	437	4.2	934	4.2	
Ventricle	97	1.7	151	1.5	263	1.2	
Cerebrum	277	4.8	470	4.5	1129	5.0	
Brain NOS	359	6.3	582	5.6	1636	7.3	
Histology							
Astrocytoma, NOS (WHO I and II)	706	12.3	1091	10.5	2260	10.1	
Anaplastic astrocytoma (WHO III)	599	10.4	993	9.5	1792	8.0	
GBM (WHO IV)	3094	53.9	5868	56.4	12,714	56.7	
Protoplasmic/fibrillary Astrocytoma	87	1.5	137	1.3	421	1.9	
Unique astrocytoma variants	34	0.6	48	0.5	96	0.4	
Ependymoma	172	3.0	298	2.9	563	2.5	
Mixed glioma	226	3.9	412	4.0	720	3.2	
Glioma, NOS	369	6.4	662	6.4	1570	7.0	
Oligodendroglioma	325	5.7	653	6.3	1714	7.6	
Anaplastic oligodendroglioma	124	2.2	250	2.4	569	2.5	
Laterality							
lpsilateral	5673	98.9	10325	99.2	22,291	99.4	
Bilateral	35	0.6	48	0.5	64	0.3	
Paired, unknown laterality	28	0.5	39	0.4	64	0.3	

CCR, California Cancer Registry; GBM, glioblastoma multiforme; LA, Los Angeles County; NOS, not otherwise specified; SEER, National Cancer Institute's Surveillance, Epidemiology, and End Results; WHO, World Health Organization.

U.S. population-based cancer registries that participate in the SEER program were included for the entire time period from 1992 to 2006. The registries were those serving the entire states of Connecticut, Hawaii, Iowa, New Mexico, Utah, and the metropolitan areas of Atlanta (Georgia), Detroit (Michigan), San Francisco-Oakland (California), Seattle-Puget Sound (Washington), Los Angeles (California), San Jose-Monterey (California), rural Georgia, and the Alaska Native Tumor Registry. SEER program registries routinely collect cancer patient demographic and medical records including primary tumor size, tumor site and histology, and stage of disease at time of diagnosis. The population

covered by the SEER program is comparable to the general U.S. population with regard to the socioeconomic status and education level, with somewhat higher proportions of foreign-born and more living in urban areas (5). Data were also obtained from the Los Angeles Cancer Surveillance Program (LAC), the populationbased SEER program registry that covers Los Angeles County, California (the SEER file that was used does not include LAC). Those data were used to evaluate the trends of incidence by age, gender, race/ethnicity, tumor site, histological subtype, and tumor laterality. The statewide California Cancer Registry (CCR), which includes LAC, was also exam-

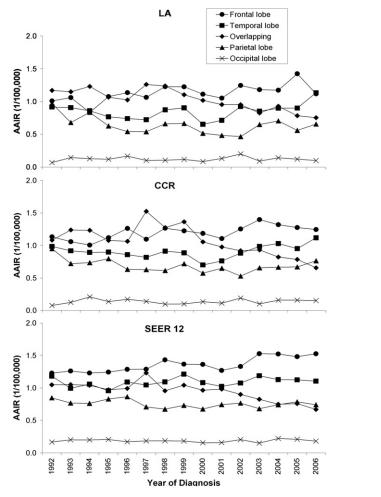


Figure 1. AAIR trends of all gliomas by anatomical subsite in 3 major cancer registries (1992 to 2006). Increased AAIRs were noted for all frontal lobe gliomas (+1.4% to +1.7% APC, $P \le 0.012$). A trend toward increased AAIR was also noted for temporal lobe lesions (+0.5% to +0.9%), although this did not reach statistical significance. Decreases in AAIRs were noted for gliomas located in overlapping regions (-2.9% to -3.6% APC, $P \le 0.002$). AAIR, age-adjusted incidence rates; APC: annual percent changes.

Patients with histologically confirmed primary CNS gliomas diagnosed between 1992 and 2006 were included (**Table 1**). CNS glioma was defined by the International Classification of Disease for Oncology, third edition (ICDO-3) topography codes C71.0–C71.9 and histology codes 9380–9480. Patients with pilocytic astrocytoma (histology code of 9421), neuroepithelial lesions (histology codes of 9381, 9423, 9430, 9444), and choroids plexus neoplasms (histology code of 9390) were excluded from the study.

Data were examined by histological subtype, subsite, and tumor size. Histological subtypes included were glioblastoma multiforme (World Health Organization [WHO] IV, ICDO-3 histology codes 9440, 9441, 9442), anaplastic astrocytoma (WHO III, ICDO-3 histology codes 9401, 9411), and lowgrade astrocytoma (WHO I and II, ICDO-3 histology code 9400). Subsite was defined as ICDO-3 topographic codes (C71.0 - Cerebrum, C71.1 - Frontal lobe, C71.2 - Temporal lobe, C71.3 - Parietal lobe, C71.4 - Occipital lobe, C71.5 - Ventricle, Not otherwise specified, C71.6-Cerebellum, Not otherwise specified, C71.7 - Brain stem, C71.8 - Overlapping lesion of brain, C71.9 - Brain, Not otherwise specified).

The annual age-adjusted incidence rate (AAIR) was calculated for each brain tumor histologic subtype and subsite for the 3 registry groups from 1992 to 2006 using SEER*Stat 6.5.2 (Seer*Stat, version 6.5.1, April 2009; http://seer.cancer.gov/seerstat/), and the 2000 U.S. standard population was used for age standardization in 5-year age groups. Annual percent changes (APC) in AAIRs were then calculated, and significance in AAIR trends was assessed using join-point analysis (Joinpoint Regression Program, version 3.3, April 2008). http:// seer.cancer.gov/resources/). We considered a 2-sided P < 0.05 as statistically significant. LAC data contain more detailed patient demographic and tumor characteristic data, including census tract of diagnosis. We performed Poisson regression analysis to assess the trends adjusting for potential confounders in LAC data. We included the following factors in the Poisson regression model by fitting a model using dichotomous or ordinal values: age (o to 19, 20 to 64, 65+ years), gender, race/ethnicity (non-Hispanic white, Hispanic white, African American, and Asian/other), and socioeconomic status

Table 2. Annual Percent Change of all Gliomas by Brain Region in 3 Major Cancer Registries, 1992 to 2006

	L	AC	CCR		SEER 12	
Brain Region	APC	<i>P</i> Value	APC	<i>P</i> Value	APC	P Value
Frontal	+1.7%	0.012	+1.4%	0.004	+1.6%	< 0.001
Temporal	+0.9%	NS	+0.7%	NS	+0.5%	NS
Parietal	-2.0%	NS	-1.3%	NS	-0.7%	NS
Occipital	+0.6%	NS	+1.4%	NS	+0.0%	NS
Overlapping	-3.1%	< 0.001	-3.6%	0.002	-2.9%	< 0.001
Ventricle	-4.2%	0.055	-4.4%	0.011	-3.7%	0.046
Cerebellum	+0.4%	NS	+0.2%	NS	-3.4%	0.014
Brainstem	-1.3%	NS	-1.1%	NS	-0.6%	NS
Cerebrum	-3.9%	0.039	-3.1%	0.016	-1.1%	NS
Brain, NOS	-2.4%	0.064	-2.7%	0.013	-3.3%	< 0.001
All sites	-0.8%	0.034	-0.8%	0.006	-0.5%	0.004

APC, annual percent changes; CCR, California Cancer Registry; LAC, Los Angeles County; NOS, not otherwise specified; NS, not significant; SEER, National Cancer Institute's Surveillance, Epidemiology, and End Results.

(high, medium, and low). Socioeconomic status was developed by LAC described elsewhere (12, 13). SAS statistical software (SAS, version 9.1. Cary, NC, USA: SAS Institute, 2002–2003) was used for all regression analysis.

RESULTS

Overall Demographics

The numbers of reported histologically confirmed cases were 5736 (LAC), 10,412 (CCR), and 22,419 (SEER). Patient demo-

Table 3. Annual Percent Change of GBM by Brain Region in 3 Major Cancer Registries, 1992–2006

	LAC		CCR		SEER 12	
Brain Region	APC	<i>P</i> Value	APC	P Value	APC	<i>P</i> Value
Frontal	+3.0%	0.001	+2.4%	< 0.001	+2.5%	<0.001
Temporal	+2.3%	0.010	+1.9%	0.026	+1.3%	0.027
Parietal	-0.5%	NS	+0.1%	NS	+0.3%	NS
Occipital	-1.2%	NS	+0.6%	NS	+0.5%	NS
Overlapping	-2.1%	0.006	-2.8%	0.015	-2.0%	0.013
Ventricle	N/A	N/A	N/A	N/A	-3.8%	NS
Cerebellum	N/A	N/A	+11.9%	< 0.001	+1.6%	NS
Brainstem	N/A	N/A	N/A	N/A	-2.7%	NS
Cerebrum	-5.4%	NS	-1.4%	NS	+0.6%	NS
Brain, NOS	+0.2%	NS	-0.0%	NS	-1.7%	NS
All sites combined	+0.5%	NS	+0.3%	NS	+0.4%	NS

APC, annual percent changes; CCR, California Cancer Registry; GBM, glioblastoma multiforme; LAC, Los Angeles County, NOS, not otherwise specified; N/A, not significant; NS, not significant; SEER, National Cancer Institute's Surveillance, Epidemiology, and End Results.

graphic characteristics for the 3 registries analyzed are highlighted in Table 1. Distributions of age and sex were similar, and the male/female ratio remained relatively constant across all 3 registries analyzed (1.2, 1.3, 1.3 for LAC, CCR, and SEER, respectively). Therefore, data were analyzed for male and female subjects combined. Significant differences in race/ethnicity were noted among the 3 registries, with a greater proportion of non-Hispanic white subjects in SEER data than in both CCR and LAC (83% vs. 65% vs. 59%, respectively). This difference is likely a result of the higher ethnic diversity in California and Los Angeles County than in the nation as a whole. Finally, no major differences in tumor location, histological subtype, or tumor laterality were noted when comparing the 3 registries.

Tumor Type

All Gliomas. The combined AAIRs of all gliomas in all 3 registries decreased over the study period, ranging between -0.5% and -0.8% APC (P \leq 0.034) (**Table 2**). However, increases in AAIR were noted for all frontal lobe gliomas (+1.4% to +1.7% APC, $P \le 0.012$) (**Figure 1**). A trend toward increased AAIR was also noted for temporal lobe lesions (+0.5% to +0.9% APC), although this did not reach statistical significance. No statistically significant changes were noted for the parietal or occipital lobes, and decreases in AAIRs were noted for gliomas located in overlapping regions (-2.9% to -3.6% APC, P \leq 0.002). AAIRs of all cerebellar gliomas were also noted to be decreased in SEER (-3.4% APC, P = 0.014).

Glioblastoma Multiforme (WHO IV)

The overall incidence of glioblastoma multiforme (GBM) in the frontal lobes increased in all 3 registries (+2.4% to +3.0% APC, $P \le 0.001$) over the time period 1992 to 2006 (**Table 3**). Furthermore, an increase in temporal lobe GBM was noted (+1.3% to +2.3% APC, $P \le 0.027$) as well (**Figure 2**). No statistically significant trends were observed for GBM in the parietal or occipital lobes. Increased AAIRs in cerebellar GBMs were noted in both CCR (APC +11.9%) and SEER (APC +1.6%), although this only reached statistical significance in the CCR data (P < 0.001). A decrease in the AAIRs of GBM located in overlapping regions was

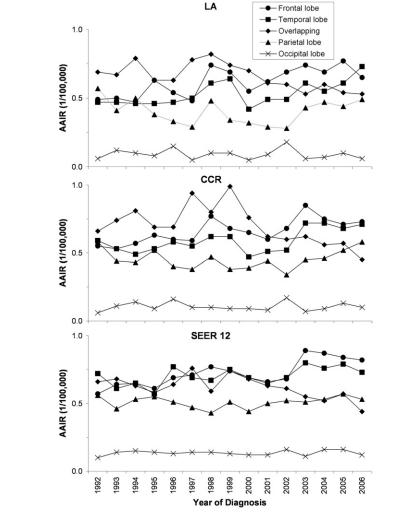


Figure 2. AAIR trends of GBMs by anatomical subsite in 3 major cancer registries (1992 to 2006). The AAIR of GBM increased in the frontal lobes (+2.4% to +3.0% APC, $P \le 0.001$) and temporal lobes (+1.3% to +2.3% APC, $P \le 0.027$) in all 3 registries. No statistically significant trends were observed in the parietal or occipital lobes. A decrease in AAIRs was observed in overlapping regions in all 3 registries (-2.0% to -2.8% APC, $P \le 0.015$). AAIR, age-adjusted incidence rates; APC, annual percent changes; GBM, glioblastoma multiforme.

noted in all 3 registries (-2.0% to -2.8% APC, $P \le 0.015$).

Anaplastic Astrocytoma (WHO III)

A notable decrease in the AAIR of frontal lobe anaplastic astrocytoma (AA) was observed, yet this reached statistical significance only in LAC (-4.5% APC, P = 0.01) (**Table 4**). A decrease in temporal lobe AA was noted in all 3 registries (APC was -3.8%, -4.2%, and -2.8%, for LAC, CCR, and SEER, respectively), but only the CCR reached statistical significance (P = 0.028). Finally, a decrease in overlapping region AA

was noted in all 3 registries (-3.4% to -9.6% APC, $P \le 0.021$).

Low-Grade Astrocytoma (WHO I and II)

Decreases in the AAIR of low-grade astrocytoma were observed in the frontal lobe region (-4.1% to -7.7% APC, $P \le 0.016$) (**Table 5**). In the temporal lobe, decreased AAIRs were observed only in SEER (-5.5%, P = 0.002). In the parietal lobe, significantly decreased AAIRs were noted in all 3 registries (-6.6% to -9.7% APC, $P \le 0.009$). Finally, decreased AAIRs were noted for overlapping region low-grade as-

trocytoma in all 3 registries (-7.3% to -8.5% APC, $P \le 0.003$).

Tumor Size

Analysis of tumor size into groups <4 cm and ≥ 4 cm demonstrated significant increases in both groups of tumors in all registries. For smaller tumors (<4 cm), APCs demonstrated statistically significant increases in all 3 registries (APC +1.4% to +3.7%). For larger tumors (≥ 4 cm), APCs were significantly increased in all 3 registries as well (APC +1.2% to +2.6%). APCs in the unknown tumor size group in all 3 registries decreased (APC -4.8% to -5.3%).

DISCUSSION

In the current study, incidence data from 3 large cancer registries were analyzed to identify trends in histologically confirmed primary CNS gliomas by histological subtype and anatomic location between the years 1992 and 2006. Although the overall incidence of primary malignant brain tumors decreased over the time period, significant increases in the AAIRs of frontal (APC +2.4% to +3.0%, P \leq 0.001) and temporal (APC +1.3% to +2.3%, P \leq 0.027) lobe GBMs were observed across all registries. Furthermore, increased AAIRs were noted in cerebellar GBMs as well, according to CCR data (APC +11.9%, P <0.001). In the parietal and occipital lobe, however, no statistically significant changes in GBM incidence were observed. Additionally, decreased AAIRs of low-grade astrocytoma and AA were observed in the majority of brain regions, and significantly decreased AAIRs of all glioma subtypes, including GBM, were noted to occur in overlapping regions in all 3 registries.

Annual percent increases in the AAIRs of frontal/temporal lobe and cerebellar GBM, yet in no other regions of the brain, coupled with the observed decreases in lower grade astrocytoma and AA incidences in these same regions, suggest a real increase in the absolute incidence of gliomas in these regions. The increased trends of AAIRs for frontal and temporal lobe GBM remained statistically significant after adjusting for age, gender, race/ethnicity, and socioeconomic status in LAC. The environmental or genetic explanations for such an observation remain speculative at this time. Future studies are clearly required to determine whether any environmental factors

Table 4. Annual Percent Change of AA by Brain Region in 3 Major Cancer Registries, 1992 to 2006

	LAC		CCR		SEER 12	
Brain Region	APC	<i>P</i> Value	APC	<i>P</i> Value	APC	P Value
Frontal	-4.5%	0.010	-2.1%	NS	-0.9%	NS
Temporal	-3.8%	0.085	-4.2%	0.028	-2.8%	NS
Parietal	-7.2%	0.053	-5.1%	0.039	-3.2%	0.066
Occipital	N/A	N/A	N/A	N/A	+1.9%	NS
Overlapping	-9.6%	< 0.001	-8.1%	< 0.001	-3.4%	0.021
Ventricle	N/A	N/A	N/A	N/A	N/A	N/A
Cerebellum	N/A	N/A	N/A	N/A	N/A	N/A
Brainstem	N/A	N/A	N/A	N/A	N/A	N/A
Cerebrum	-0.5%	NS	-3.6%	NS	-2.2%	NS
Brain, NOS	N/A	N/A	-13.7%	< 0.001	-10.0%	< 0.001
All sites combined	-5.6%	< 0.001	-4.7%	< 0.001	-2.9%	< 0.001

AA, anaplastic astrocytoma; APC, annual percent changes; CCR, California Cancer Registry; LAC, Los Angeles County; NOS, not otherwise specified; N/A, not significant; NS, not significant; SEER, National Cancer Institute's Surveillance, Epidemiology, and End Results.

Table 5. Annual Percent Change of Low-Grade Gliomas (WHO II) by Brain Region in 3 Major Cancer Registries, 1992 to 2006

	L	LAC		CCR		SEER 12	
Brain Region	APC	P Value	APC	P Value	APC	P Value	
Frontal	-7.7%	0.016	-7.0%	0.004	-4.1%	0.009	
Temporal	-4.3%	NS	-4.4%	NS	-5.5%	0.002	
Parietal	-9.7%	0.006	-8.3%	0.009	-6.6%	< 0.001	
Occipital	N/A	N/A	N/A	N/A	-7.1%	0.079	
Overlapping	-7.3%	0.003	-7.9%	< 0.001	-8.5%	< 0.001	
Ventricle	N/A	N/A	N/A	N/A	N/A	N/A	
Cerebellum	N/A	N/A	-6.1%	0.05	-12.4%	< 0.001	
Brainstem	N/A	N/A	N/A	N/A	-10.2%	< 0.001	
Cerebrum	-7.8%	0.025	-8.9%	0.019	-7.2%	0.058	
Brain, NOS	N/A	N/A	-7.6%	0.022	-6.6%	0.003	
All sites	-6.7%	< 0.001	-6.6%	< 0.001	-6.5%	< 0.001	

APC, annual percent changes; CCR, California Cancer Registry; LAC, Los Angeles County; NOS, not otherwise specified; N/A, not significant; NS, not significant; SEER, National Cancer Institute's Surveillance, Epidemiology, and End Results; WHO, World Health Organization.

are related to the observed anatomical incidence trends in this report.

A potential explanation of our findings is an effect of diagnostic bias accompanying the increased volume of neuroimaging that has occurred over the last 2 decades. It is well known that gliomas have a preponderance for originating in the frontal and temporal lobes, even after adjusting for differences in the surface areas of these regions (2, 10). The observations in this study may therefore be a byproduct of significant increases in diagnostic imaging use and sensitivity, such as computed tomography and

magnetic resonance imaging, occurring worldwide over the last 2 decades (15, 17). As more routine imaging studies are performed and more lesions are diagnosed incidentally, the observed proportions of lesions located in the frontal and temporal lobes may increase as they approach the absolute proportion of gliomas located in each region in the general population. Furthermore, tumors originating in the frontal lobes may have a tendency to remain clinically silent and not come to medical attention for a longer time period than tumors in other locations. It is therefore possible that rapid increases in the volume of brain imaging have caused more clinically silent and possibly smaller lesions to be diagnosed at an earlier stage than larger, overlapping region tumors that may come to clinical attention at an earlier time. The decreased AAIRs of overlapping brain lesions in all 3 major tumor registries for all histological subtypes lends some support to this explanation. However, our analysis of tumor size at the time of diagnosis did not suggest a trend toward smaller tumor size at diagnosis, which would be expected if more tumors were being diagnosed at earlier growth stages.

Although less likely, yet another potential explanation for the observed trends in tumor topography in the current study is a change in coding practices of anatomic locations or histologic subtypes for gliomas over the time period analyzed. Previous studies have reported high-quality consistency for ICD-o coding of primary malignant brain tumors, with the exception of mixed gliomas and unspecified tumors (3). Additionally, all cases included in the current study were histologically confirmed lesions, reducing the effect introduced by a potential increase in empiric treatment for incidentally diagnosed lesions. The decreased AAIRs of low-grade astrocytoma and AA in these registries may lend support to the idea that changes in WHO criteria or improvements in histopathological techniques for diagnosing GBM may have caused more tumors to be included in this more malignant category. It is also possible that decreased AAIRs of lower-grade lesions were observed because they were instead designated as related entities such as oligodendroglioma. A separate analysis, however, did not reveal a steady increase in the diagnosis of WHO grade II or III oligodendroglioma over the same time period in any brain region (data not shown).

The analysis by tumor size showed significant decreases in the incidence of unknown size, whereas all other size categories showed increased incidence rates. These observations may suggest improved reporting and coding practices over the last 2 decades. However, if this phenomenon held true for the observations in anatomical location data, it would therefore be expected that this effect would occur in the other lobes of the brain as well; the AAIRs of GBM in the parietal and occipital lobes did not change significantly over the last 15 years, whereas notable increases were observed in the frontal and temporal lobes.

Finally, other possible explanations for observed trends could be from changes in environmental factors, natural variations over time, ICD9 coding of operable versus inoperable tumors, and lower thresholds in the use of magnetic resonance imaging for patients with mild symptoms.

CONCLUSIONS

A review of 3 large cancer registries over a 15-year period showed overall decreased rates of primary malignant brain tumors in all sites, with the notable exceptions of increased incidence of GBM in the frontal lobes, temporal lobes, and cerebellum. Although these results may represent an effect of diagnostic bias or refinements in anatomical subsite coding, an environmental cause of the increases of highgrade frontal and temporal lobe malignancies cannot be ruled out. Further studies are indicated to establish whether a correlation with environmental factors exists.

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